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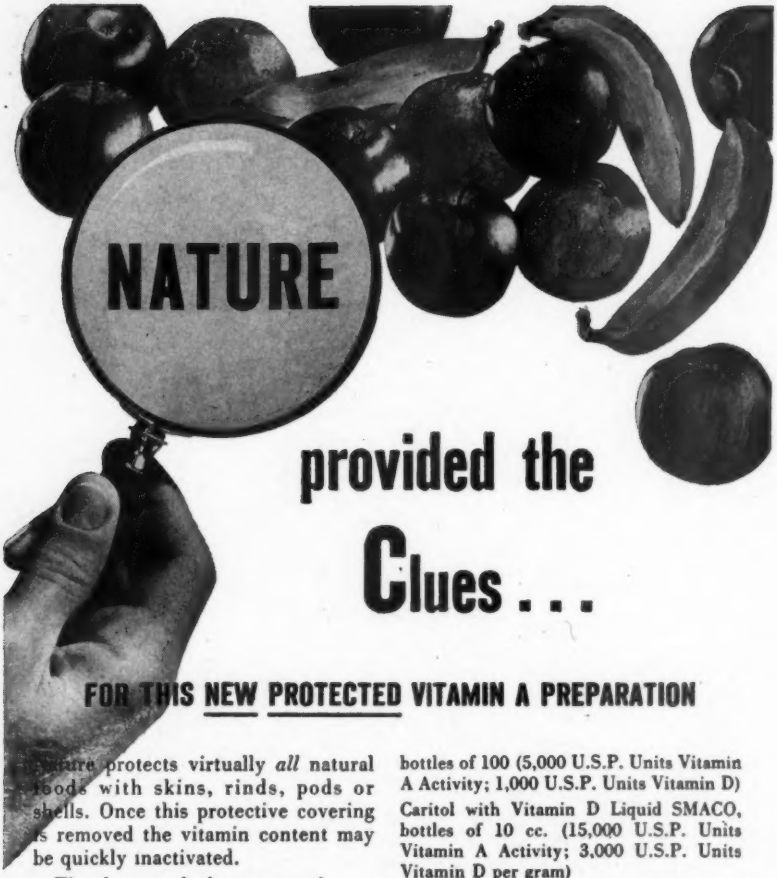

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CONTENTS

PAGE

Editorial:

Sulfanilamide, Penicillin, ————? 2

Articles:

Sulfonamides and Phagocytosis. By Louis Gershenfeld and M. J. Silver 4

The Fiftieth Anniversary of the Death of John Michael Maisch. By George Urdang 14

Inflationary Borrowing. By Karl Scholz 25

Rationing, Our Diet, and Sound Nutrition. By T. Swann Harding .. 28

Selected Abstracts 37

Solid Extracts 41

Book Reviews 43

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E D I T O R I A L

SULFANILAMIDE, PENICILLIN, ———?

PROBABLY no other substance has aroused more interest in medical and pharmaceutical circles than penicillin. It is of course true that Domagk's research on prontosil was and will always be one of the landmarks in the history of chemotherapy, but at that time no one could quite visualize all the progress that was to be painstakingly made in the last decade in the development of this group of drugs. With penicillin the circumstances are quite different. First the specific effectiveness of the sulfonamides had led many of us to believe that the day of botanical drugs was past and that only organic synthesis could produce the "super" drugs of the future. Large manufacturing companies were curtailing their activities in the field of galenicals and planning a future made up predominantly of synthetics in tablet and injection form to replace the wide diversity of products of the past from natural sources. Research was directed principally to the preparation and pharmacologic study of literally thousands of new derivatives, largely the products of organic synthesis.

The developments on penicillin will not in any sense stop this type of work since many great discoveries are undoubtedly waiting to be uncovered in this field. They have, however, broadened our vision to include the possibilities of new drugs from plant and animal sources as yet unknown and given us renewed respect for research in these fields.

We can learn but little of the painstaking work that is being directed toward the elaboration of the structure of penicillin since it is considered as a war secret. There is however no doubt but that every effort is being made to do this as a prelude to its synthesis. The current methods for its production by culture and extraction are time consuming, tedious and inefficient and yet it is quite possible that it may defy all efforts to synthesize it as have insulin, quinine and other drugs of primary importance still obtained only from natural sources.

If our chemists are successful in determining the structural formula of penicillin who can predict the profound changes in its activity that might be produced by slight changes in its substituent groups? A host of new chemotherapeutic substances may result, some with even better action than penicillin itself.

The most striking thing about penicillin is its almost complete lack of toxicity. In the early days of sulfonamide therapy toxicity was very often forgotten since the patient's condition was frequently such that death would probably ensue if it were not used and toxicity was simply a chance that was taken. Today proper sulfonamide therapy requires careful laboratory control since toxicity is a factor that is always present in the background and still it occasionally causes death.

Penicillin shows very little toxicity and few if any deaths can be attributed to its use. In this respect it is the nearest approach to the ideal propounded by Ehrlich that we have as yet achieved.

Clinical reports on the effectiveness of penicillin have shown it to be very valuable in a number of infections for some of which we have no other effective means of control, *e. g.* osteomyelitis, and yet it is not effective in every type of infection.

It does not, however, seem at all presumptuous to believe that all infections will some day be subject to rigid control with many of them completely eradicated from the human race. This is not now nearly as far-fetched as it seems. Although it does not become those of us in the medical sciences to suggest it, it does seem unfortunate that the progress of the social and political sciences has not kept abreast us. It will indeed be a happy day when it is our duty to patch a man's wounds not that he may simply fight or work again but that he may live and live abundantly.

L. F. Tice

SULFONAMIDES AND PHAGOCYTOSIS

By Louis Gershenfeld and Melvin J. Silver*

Introduction

TWO of the most outstanding developments in the history of medical science are the discovery of the role of phagocytosis as a normal defense mechanism of the body and the discovery of the therapeutic efficiency of the sulfonamide drugs.

Previous to the year 1884 Panum, Roser, Koch and Sternberg made statements which anticipated the theory of phagocytosis. Their observations, however, were inadequate and were not proven by research. It remained for Elie Metchnikoff in 1884 to present satisfactory scientific evidence and to champion the theory of phagocytosis, a theory which, although modified by our later knowledge of the importance of the humoral elements in immunity, remains in high esteem even today.

In 1935 Domagk (5) reported that sulfamido-chrysoidine protects mice against fatal doses of streptococci. Shortly after this discovery it was shown that the sulfamido-chrysoidine is changed within the body to sulfanilamide which is the effective chemotherapeutic agent (1, 4, 10, 24). What happened following this is common knowledge and the sulfonamide drugs are established today as effective and desirable chemotherapeutic agents.

The most plausible theories in the present controversy concerning the mechanism of the bacteriostatic activity of the sulfonamide drugs are presented by Woods (31), Fildes (7), Woods and Fildes (32), West and Coburn (30), Selbie (22), Green (12), Dorfman *et al.* (6), Findlay (8), Finkelstein and Birkeland (9), Stamp (23), Gay *et al.* (11), McIntosh *et al.* (14), Johnson (13), and Rubbo and Gillespie (18, 19). In best repute today is the theory of Woods (31) who holds that sulfanilamide competes for an enzyme which reacts on para-amino-benzoic acid (an essential metabolite of the

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bacterial cell). Due to the close chemical relationship between sulfanilamide and para-amino-benzoic acid, the sulfanilamide displaces para-amino-benzoic acid in the enzyme reaction and bacteriostasis ensues.

A good chemotherapeutic agent should enhance or at least not reduce the efficiency of the normal defense mechanisms of the infected host (28). It is therefore evident that agents which inhibit the amount and degree of phagocytosis must be impeding a normal defense mechanism of the body and so manifest their toxicity to the blood tissue.

It is the purpose of this investigation to show by a number of *in vitro* experiments the effect of six widely used sulfonamide compounds on phagocytosis by human leucocytes.

Investigation

The method employed in this study is essentially the phagocytic test of Welch and Hunter (28) with certain specified modifications.

Materials:

Human Blood—Five cc. of blood are withdrawn from the arm by venipuncture and immediately mixed well with 0.2 cc. of 20 per cent sodium citrate in isotonic salt solution to give a final concentration of 0.78 per cent citrate. The blood was always used in the tests within two hours after withdrawal.

The Antigen—The stock antigen was prepared as described by Welch and Hunter (28) using ferric alum for artificial opsonization. The stock antigen was not used if it was older than one month. For use in the tests the stock antigen was carefully diluted to give a turbidity equivalent to the number 2 McFarland nephelometer standard or a bacterial count of 600,000,000 staphylococci per cc.

The Sulfonamide Compounds—The following sulfonamide compounds, in aqueous solutions, with the respective final concentrations as mentioned, were employed:

Chemical	Final Dilution	Final Concentration in mg./100 cc.
1. Sulfanilamide (Merck)		
	A—1/625	151
	B—1/10,000	10
	C—1/50,000	2
	D—1/100,000	1
2. Sulfapyridine (Merck)		
	A—1/17,500	5
	B—1/50,000	2
	C—1/250,000	0.4
	D—1/500,000	0.2
3. Sulfathiazole (Lilly)		
	A—1/8,500	12
	B—1/25,000	4
	C—1/100,000	1
	D—1/500,000	0.2
4. Sulfadiazine (American Cyanamide Co.)		
	A—1/65,000	1.5
	B—1/100,000	1
	C—1/250,000	0.4
	D—1/500,000	0.2
5. Sulfaguanidine (Sharp & Dohme)		
	A—1/5,000	20
	B—1/50,000	2
	C—1/250,000	0.4
	D—1/500,000	0.2
6. Succinylsulfathiazole (Sharp & Dohme)		
	A—1/65,000	1.5
	B—1/100,000	1
	C—1/200,000	0.5
	D—1/400,000	0.25

In each case the final dilution of the A sample represents the greatest concentration of the particular sulfonamide that can be obtained starting with a saturated solution of the sulfonamide under the conditions of the test.

Experimental Procedure:

The following materials were pipetted into the bottom of 100 by 13 mm. test tubes:

(1)—0.2 cc. of desired sulfonamide dilution.*

(2)—0.4 cc. of citrated fresh human blood.

(3)—0.4 cc. of standardized antigen suspension.

After the addition of (2), the tubes were shaken gently and again after the addition of (3). A control was prepared with every experiment. The control received the blood and the antigen and 0.2 cc. of sterile distilled water instead of 0.2 cc. of the sulfonamide dilution. The tubes with contents were stoppered with rubber stoppers previously treated with dilute alkali and then neutralized to remove material toxic to blood. The stoppers employed were selected to fit the mouths of the tubes tightly so that no space existed between the portion of the stopper protruding into the tube and the wall of the tube. It was observed that a large portion of the mixture became ensnared in this space when the end of the stopper did not fit the mouth of the tube tightly and thus adequate mixture of the whole sample was not insured.

Finally the tubes were placed on the rotating machine and rotated for thirty minutes at four revolutions per minute in the incubator at 37° C. The tubes were then removed from the rotating machine and a portion of the well-mixed contents of each tube was removed with a capillary pipette and blood smears were made. The smears were stained with 1 per cent methylene blue in absolute methyl alcohol as suggested by Welch and Hunter (28). The number of staphylococci phagocytosed by each of twenty-five polymorphonuclear leucocytes were counted and recorded as follows:

* Desired dilution is five times as concentrated as the final dilution.

— no phagocytosis, no staphylococci ingested.
+ slight phagocytosis, 1-20 staphylococci ingested.
++ moderate phagocytosis, 20-40 staphylococci ingested.
+++ marked phagocytosis, over 40 staphylococci ingested.

Table I

Showing the % of leucocytes with no phagocytosis, slight, moderate, and marked phagocytosis resulting from treatment with each sulfonamide dilution and the controls under the conditions of the test.

Compound and Dilution		% Phagocytosis			
		—	+	++	+++
Sulfanilamide					
A. 1/625	(aver. of 8 exps.)	17	59.5	12	11.5
B. 1/10,000	(aver. of 8 exps.)	15	63.5	15	6.5
C. 1/50,000	(aver. of 8 exps.)	16.5	64	13	6.5
D. 1/100,000	(aver. of 8 exps.)	13.4	71.3	10	5.3
Control	(aver. of 6 exps.)	21.3	66.7	8.7	3.3
Sulfapyridine					
A. 1/17,500	(aver. of 7 exps.)	28	67.3	3.4	1.3
B. 1/50,000	(aver. of 6 exps.)	28.7	66	4.6	0.7
C. 1/250,000	(aver. of 6 exps.)	25.3	69.4	5.3	0
D. 1/500,000	(aver. of 6 exps.)	28	66	6	0
Control	(aver. of 6 exps.)	19.3	71.3	6.7	2.7
Sulfathiazole					
A. 1/8,500	(aver. of 9 exps.)	11	74	9	6
B. 1/25,000	(aver. of 8 exps.)	9.5	74	11	5.5
C. 1/100,000	(aver. of 8 exps.)	12	71	8.5	8.5
D. 1/500,000	(aver. of 7 exps.)	12	71	9	8
Control	(aver. of 8 exps.)	17.5	69	9	4.5
Sulfadiazine					
A. 1/65,000	(aver. of 6 exps.)	15.4	70.6	10.7	3.3
B. 1/100,000	(aver. of 6 exps.)	12.7	66.6	14.7	6
C. 1/250,000	(aver. of 6 exps.)	9.3	74	9.3	7.4
D. 1/500,000	(aver. of 6 exps.)	10.7	74.6	10.7	4
Control	(aver. of 6 exps.)	24	68	6.7	1.3
Sulfaguanidine					
A. 1/5,000	(aver. of 8 exps.)	25	70.5	4.5	0
B. 1/50,000	(aver. of 8 exps.)	24.5	71	4.5	0
C. 1/250,000	(aver. of 7 exps.)	24	72.6	2.8	0.6
D. 1/500,000	(aver. of 7 exps.)	27.5	67.4	4.5	0.6
Control	(aver. of 8 exps.)	20	73.5	6.5	0
Succinylsulfathiazole					
A. 1/65,000	(aver. of 6 exps.)	19.3	78	2.7	0
B. 1/100,000	(aver. of 6 exps.)	18.7	78	3.3	0
C. 1/200,000	(aver. of 6 exps.)	20	76.7	3.3	0
D. 1/400,000	(aver. of 6 exps.)	22	74.7	3.3	0
Control	(aver. of 6 exps.)	16	79.3	4	0.7

Table II

Showing the % increase and % decrease of leucocytes showing no phagocytosis (—), moderate phagocytosis (++), and marked phagocytosis (+++) caused by each particular sulfonamide dilution.

Chemical	% Leucocytes Showing — Increase	% Leucocytes Showing — Decrease	% Leucocytes Showing ++ Increase	% Leucocytes Showing ++ Decrease	% Leucocytes Showing +++ Increase	% Leucocytes Showing +++ Decrease
Sulfanilamide						
A. 1/625		4.5	3.5		8	
B. 1/10,000		6	6		3	
C. 1/50,000		5	4.5		3	
D. 1/100,000		8	1.5		1	
Sulfapyridine						
A. 1/17,500	9			3		1.5
B. 1/50,000	9.5			2		2
C. 1/250,000	6.5			1.5		2.5
D. 1/500,000	8.5			1		2.5
Sulfathiazole						
A. 1/8,500		6.5	0		2	
B. 1/25,000		8	2		1	
C. 1/100,000		5.5		*	4	
D. 1/500,000		5.5	*		3.5	
Sulfadiazine						
A. 1/65,000		8.5	4		2	
B. 1/100,000		11.5	8		4.5	
C. 1/250,000		14.5	2.5		6	
D. 1/500,000		13	3.5		2.5	
Sulfaguanidine						
A. 1/5,000	5			2		0
B. 1/50,000	4.5			2		0
C. 1/250,000	4			4	*	
D. 1/500,000	7.5			2	*	
Succinylsulfathiazole						
A. 1/65,000	3			1.5		1
B. 1/100,000	2.5			1		1
C. 1/200,000	4			*		*
D. 1/400,000	6			*		*

* Indicates less than 1%.

Results

Table I contains in tabulated form data which we also have available in graphs. Table II consists of a tabulation of the per cent increase or per cent decrease in the various degrees of phagocytosis recorded (none, slight, moderate, and marked) caused by each sulfonamide dilution tested. In Table II we note that the sulfonamide drugs in the dilutions considered may be divided into two general groups according to their effect on the phagocytic action of human leucocytes. In the first group are found sulfanilamide, sulfathiazole and sulfadiazine which cause a slight decrease in the per cent of leucocytes showing no phagocytosis and a variable increase in the per cent of leucocytes showing moderate and marked phagocytosis. The second group, on the other hand, consisting of sulfapyridine, sulfaguanidine and succinylsulfathiazole causes a slight increase in the per cent of leucocytes showing no phagocytosis and a negligible decrease in the per cent of leucocytes showing moderate and marked phagocytosis.

Although these changes are small (14.5 per cent being the greatest and averaging about 5 per cent), it is of interest to note that they occurred constantly. This is borne out by the graphs which represent average determinations from over 160 experiments.

Discussion

Tunnicliff (25) noted that prontosil soluble (disodium-4′ sulfamidophenyl-2-azo-7-acetylamino-1-hydroxynaphthalene-3,6 disulfonate) in dilutions of 1/1000 to 1/100,000,000 and sulfanilamide in dilutions of 1/100,000 to 1/200,000 in isotonic salt solution promote phagocytosis of the viridans and hemolytic streptococci. Finkelstein and Birkeland (9) reported that sulfanilamide and prontosil in dilutions of 1/50,000 to 1/100,000 increased both the number of hemolytic streptococci phagocytosed per leucocyte and the number of leucocytes exhibiting phagocytosis. Chandler and Janeway (3) reported a marked increase in the phagocytosis of hemolytic streptococci caused by sulfanilamide in dilutions of 1/40,000 to 1/80,000. More recently Reed and Orr (16), working with five of the six sulfonamide drugs under investigation by us, arrived at the general conclusion that sulfanilamide and its derivatives in concentrations of 8 mg./100 cc. to 80 mg./100 cc. have no effect on phagocytosis by guinea-pig leucocytes.

The results of all the above *in vitro* tests are in general agreement with our findings. The work of Reed and Orr (16) noted above was carried out with guinea-pig blood and it is highly possible that the greater resistance of human leucocytes (as compared with guinea-pig leucocytes) to the toxic effects of drugs on phagocytosis (26, 28) is also manifested by an increased susceptibility to the stimulating effect of other drugs on phagocytosis. This would explain the increase of phagocytosis by human leucocytes as compared to no effect on phagocytosis by guinea-pig leucocytes when both are under the influence of sulfanilamide, sulfathiazole and sulfadiazine.

Reed and Orr (16) also tested sulfapyridine and sulfaguanidine and found no effect on phagocytosis by guinea-pig leucocytes, whereas we found that these drugs decrease phagocytosis by human leucocytes. Welch (26) observed that a thermostable opsonin, not found in guinea-pig blood, appears to be responsible for the greater resistance of human blood to substances toxic to phagocytes. It may then be possible that substances like sulfapyridine, sulfaguanidine and succinylsulfathiazole cause a decrease in phagocytosis by human leucocytes by inactivating the thermostable opsonin present in human blood and at the same time cause no decrease in phagocytosis by guinea-pig leucocytes because this thermostable opsonin is not present in guinea-pig blood.

Bliss and Long (2) injected mice intraperitoneally with hemolytic streptococci and *Clostridium welchii* and then injected a solution of sulfanilamide. Mice injected with sulfanilamide showed increased phagocytosis in the peritoneal exudate as compared with controls.

Welch *et al.* (29) concluded that sulfanilamide stimulated the opsonocytophagic power of the blood of *Brucella* infected guinea pigs.

Reed and Orr (16) inoculated guinea-pig wounds with *Clostridium welchii* and *Clostridium sordelii* and treated them locally with 15 grams of sulfathiazole four hours later. At intervals of four to ten hours after infection, they removed samples of the exudate by inserting fine capillary tubes into the lumens of the wounds. They observed that more phagocytosis occurred in the wounds treated locally with sulfathiazole than in the untreated wounds.

McIntosh *et al.* (14) concluded that sulfonamides do not stimulate leucocytic or phagocytic activity as shown by the action of sulfapyridine in pneumococcic infections of mice. Sulfapyridine appears to decrease phagocytosis by human leucocytes *in vitro* and it is quite

possible that the same effect may occur in mice *in vivo,* but it is dangerous to make a generalization such as these workers have done on the basis of a limited group of experiments using only one of the sulfonamide drugs. In the light of our investigation and other researches mentioned above, it appears obvious that McIntosh *et al.* (14) have arrived at an unwarranted generalization.

Reed and Orr (15) treated guinea-pig wounds locally with 150 mg. of sulfathiazole and found that the wound exudate remained supersaturated with the drug for over twenty-four hours and the musculature of the remainder of the leg retained 30 to 5 mg. per 100 cc. for over twenty-four hours. If it may be inferred that sulfanilamide is retained in the wound exudate and in the musculature of the area surrounding the wounds of humans in quantities similar to those reported above for sulfathiazole in guinea-pig wounds, we have strong supporting evidence for the efficiency of sulfanilamide in war wounds (and which we have shown to increase phagocytosis *in vitro* in human blood).

Summary and Conclusions

The effect of six widely used sulfonamide compounds on phagocytosis by human leucocytes was determined by a modification of the Welch and Hunter (28) *in vitro* phagocytic test.

The sulfonamide compounds tested were divided into two groups on the basis of their effect on phagocytosis by human leucocytes in the dilutions tested.

Sulfanilamide in dilutions of 1/625 to 1/100,000, sulfathiazole in dilutions of 1/8500 to 1/500,000 and sulfadiazine in dilutions of 1/65,000 to 1/500,000 cause a slight decrease in the total number of human leucocytes showing no phagocytosis and a variable increase in the number of human leucocytes showing moderate and marked phagocytosis.

Sulfapyridine in dilutions of 1/17,500 to 1/500,000, sulfaguanidine in dilutions of 1/5000 to 1/500,000 and succinylsulfathiazole in dilutions of 1/65,000 to 1/400,000 (to a lesser extent) cause a slight increase in the total number of human leucocytes showing no phagocytosis and a negligible decrease in the number of human leucocytes showing moderate and marked phagocytosis.

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THE FIFTIETH ANNIVERSARY OF THE DEATH OF JOHN MICHAEL MAISCH *

By George Urdang, D. Sc.**

ALMOST to the day fifty years ago, on the tenth of September, 1893, there died at Philadelphia the first Permanent Secretary of the American Pharmaceutical Association, John Michael Maisch.

It may well be said that this position and this man were created for each other. As a matter of fact, it is very questionable whether the permanent secretaryship of the American Pharmaceutical Association would have been established in 1865 and maintained in 1870, had it not been for the conviction of those concerned that with Maisch destiny had presented to them the ideal man for such an office and that in not taking advantage of this rare opportunity they would have failed their duty.

It is significant that Maisch at first declined the nomination. He accepted after William Procter, Jr., had publicly expressed the hope "that Mr. Maisch will overlook individual feelings and preferences, and look only to the good of the Association." (1) For four years he sacrificed his time and work to this secretaryship for the almost ridiculous annual compensation of $100.00. Then, in 1869, he handed in his resignation. "I find," he motivated his decision, "that the duties are very onerous, and engross too much of my time, so that it is utterly impossible for me to serve in that capacity any longer." (2) In spite of its very limited means, the Association reacted by raising the salary of the Permanent Secretary to fourfold the previous amount, *i. e.* to $400.00, for the year 1869/70 and from then on to $500.00 annually, and the President of the A. Ph. A. for 1869/70, Ezekiel H. Sargent, in his official address directed to Maisch the following appeal:

"Knowing as we all do the many and laborious duties of his [Maisch's] position, and the self-sacrificing spirit with which he has

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** Director of the American Institute of the History of Pharmacy.

performed them, and feeling that we can have no claim upon him for further similar toil, I almost hesitate to urge him to continued service. Yet so plainly is the importance of his work seen, that I earnestly hope he may consent to further afford his valuable services in the position he is so eminently qualified to fill. I say this in the belief that as he has the good of the Association at heart, he will not decline, if it be shown that his services are necessary." (3)

Although even $500.00 were by no means an adequate payment of the work he did and the time he spent on it, Maisch naturally did "not decline."

There was a galaxy of excellent people active in the American Pharmaceutical Association at this time. The older generation, still wielding the scepter, was represented by men like the Philadelphians William Procter, Jr., and Edward Parrish and the physician-pharmacist Edward R. Squibb, of Brooklyn, N. Y. Of the younger generation the lists of those attending the meetings of the A. Ph. A. at Baltimore and Chicago in 1869 and 1870 respectively contain among others the names of Charles E. and Louis Dohme, of Baltimore, George F. H. Markoe, of Boston, Alfred B. Taylor, of Philadelphia, Albert E. Ebert, of Chicago, and S. A. D. Sheppard, of Boston. (4) Who then was the man chosen or at least recognized by these people as the one to conduct their national Association in one of the most decisive periods of American pharmaceutical organizational endeavor?

It was the German immigrant Johann (John) Michael Maisch, who was merely thirty-four years of age and who had been in this country about sixteen years when elected Permanent Secretary of the American Pharmaceutical Association.

J. M. Maisch, born on the 30th of January, 1831, at Hanau, in Southern Germany, was one of those scientists and progressives who are ready to sacrifice everything, even their lives, for both science and progress.

It is touching to learn from his autobiographical notes (5) how the ambitious youngster, whose poverty stricken parents could not afford the high tuition fees of the German high schools for children of the privileged classes, achieved free instruction and the best marks by strenuous work exceeding by far the strength of the boy, and how just this zeal defeated his purpose and caused his well meaning teachers to deny him the continuance of his studies for fear that his poor health would not stand the strain.

It is significant that the young man, although excluded from the world of learning, kept faith with the world of ideas and ideals and participated in the German revolution of 1848, the first determined attempt to establish democracy on German soil.

It is exciting to read about his escaping from the prison into which he was thrown because of his revolutionary activity, and it is heartwarming to realize that it was his flight to the United States of America that presented him with all he had longed for in the country of his birth: liberty and, in the wake of it, the opportunity of entering the field that was his by its and his very nature, the field of science and organization.

It is not the intention of this memorial to offer a complete biography of John Michael Maisch. Such a biography would exceed the limitations of a paper like this in more than one direction. It is not even intended to add another biographical sketch to those already written about this man and his work. (6) The intention is to emphasize one special part of the many activities of John M. Maisch which strangely enough has been given little attention or none at all in the biographical sketches mentioned: the decisive rôle played by Maisch in the organization and stabilization of American pharmacy by way of association and legislation. It is not the teacher, or the author, or the manufacturer, the retail pharmacist or the scientific investigator John Michael Maisch with whom this paper is concerned, but the first Permanent Secretary of the American Pharmaceutical Association.

There cannot be any doubt: it was primarily the work done by Maisch in this latter capacity that survived him.

When the eighteen year old youth arrived in the city of Baltimore in 1849, there was no idea of making use of his good background in the sciences, especially in botany and chemistry, and of any connection with pharmacy. The young immigrant started his American career as a worker in a box factory. It was by mere chance that Maisch, in 1850, became acquainted with a German physician, Dr. Wiss, who intended to open a pharmacy and furnished his talented young compatriot with literature "pertaining more or less to pharmacy." (7)

When the store was established Maisch was made its manager. Although he lost this position after only about one year when, late in 1851, the store was sold, the young man had finally found his

field of opportunity. His entire later life was devoted to pharmacy which he served in almost all of its phases.

The decision of John Michael Maisch to become an American pharmacist and the formation of the American Pharmaceutical Association happened almost simultaneously. The American Pharmaceutical Association owed its founding in 1852 primarily to the desire of the élite of American pharmacy "to improve and regulate the drug market, by preventing the importation of inferior, adulterated or deteriorated drugs, and by detecting and exposing home adulteration." (8) Two years later, in 1854, the German immigrant John M. Maisch published his first article in the American Journal of Pharmacy. Its title was "On the Adulteration of Drugs and Chemical Preparations." (9) The article was short. It was essentially a report of the young self-taught pharmacist on a substitution of carbonate of lime by sulfate of lime detected by him. Maisch concluded in advocating the more frequent execution of such investigations and the publication of their results. The significance of this article lay in the identity of purpose of the young author and the young American Pharmaceutical Association.

In 1856 Maisch joined the American Pharmaceutical Association. In 1860, only twenty-nine years of age, he became Chairman of the Committee on the Progress of Pharmacy. In 1862 he was elected Corresponding Secretary, in 1863 First Vice-President and Chairman of the Executive Committee, and finally, in 1865, he was appointed the first Permanent Secretary of the American Pharmaceutical Association. In the meantime Maisch had been a commercial analytical chemist and simultaneously Superintendent of the practical department of Parrish's School of Pharmacy for Students of Medicine (1859/60), Professor of Materia Medica at the New York College of Pharmacy and simultaneously a chemist at the manufacturing plant of Dr. E. R. Squibb in Brooklyn, N. Y. (1861/62), and from 1863 to 1865, on personal recommendation of Dr. Squibb, Superintendent of the United States Laboratory in Philadelphia. When this laboratory was closed at the end of the Civil War, Maisch opened a retail pharmacy in Philadelphia.

In the same year, 1866, the brand-new Secretary of the American Pharmaceutical Association was elected to succeed William Procter, Jr., in the chair of pharmacy in the Philadelphia College of Pharmacy. "We know," said an editorial in the American Journal

of Pharmacy very likely written by William Procter, Jr., himself, "of no one who can bring to the task involved in this appointment so large a share of practical and theoretical knowledge as Professor Maisch." (10)

The fact that William Procter, Jr., resigned at just this time was undoubtedly to some extent caused by his intention to secure the utilization of the talents of Maisch for educational as well as for organizational purposes.

Reporting on the first year of a permanent A. Ph. A. secretaryship, Henry W. Lincoln, in his presidential address delivered at the Detroit meeting of the A. Ph. A. in 1866, made the following statements:

"The new feature in the history of the Association of electing a Permanent Secretary has had only one year of trial, but sufficient benefit has already been experienced to warrant the change. . . . The action of the Philadelphia College of Pharmacy in electing him to the Chair voluntarily made vacant by the resignation of one of our oldest and valued members, is a well merited tribute to the talents and industry of our Secretary." (11)

It was at the New York A. Ph. A. meeting of 1867, only two years after the creation of the office of a Permanent A. Ph. A. Secretary, that the scene was set for the activity of John M. Maisch as the initiator and guardian of adequate pharmaceutical legislation in the United States of America.

On September 13, 1867, at the sixth session of the meeting, the Business Committee, presided over by Dr. E. R. Squibb, presented the following resolution:

"Whereas, It is recognized as a prominent means by which this Association hopes to increase its public usefulness as a national Association, to urge upon our legislators the importance of a judicious, but certain, determined, and, as far as practicable, uniform control of the practice of pharmacy in the various States; therefore,

"Resolved, That the President and Executive Committee of the Association be authorized and instructed to offer any service which the Association can render to the various conventions for reforming State Constitutions, and to State Legislatures as opportunity may arise, wherein such bodies may consider the cooperation of the Association either desirable or useful." (12)

There is no doubt of the fact that this suggested resolution was revolutionary. At this time only a small minority in American pharmacy wanted a "certain, determined, and, as far as practicable, uniform control of the practice of pharmacy in the various States." Most of the American pharmacists in the sixties and even seventies of the nineteenth century did not want any legal control of their conduct of business.

The Chairman of the Business Committee of the A. Ph. A., Dr. Squibb, found himself in a precarious situation. To him opposition to legal regulations and restrictions was a matter of principle, a consequence of his deep mistrust of politics and politicians. This resolution, however, was called for by the then President Elect of the A. Ph. A. and host of this meeting, the venerable John Milhau, on the ground of plans pending in the New York legislature to bring about some kind of pharmaceutical legislation. Dr. Squibb could not possibly deny Mr. Milhau the assistance of the Association which the old gentleman asked for. He tried, however, his utmost to localize the whole affair and "to confine the scope."

It was then and there that a kind of duel developed between Edward R. Squibb and John M. Maisch. Carefully avoiding any personal opinion, Squibb merely related that Mr. Milhau "has deemed it worthwhile to have some expression by this Association of its willingness to cooperate through its permanent officers with this organization," *i. e.* "the present Convention" planning to reform the State Constitution of New York. Immediately Maisch seconded the resolution, suggested an amendment adding "the officers of the Association" to the President and the Executive Committee as members of the group expected to deal with legislative questions, and gave an explanation definitely recognizing the national importance of the matter concerned.

The resolution was adopted in the form given to it by the amendment of Maisch, and it was on this basis that he, in his capacity as Permanent Secretary of the A. Ph. A., undertook the collection of information concerning "laws . . . now in force . . . or in consideration . . . relating in any way to the practice of pharmacy, the education of pharmacists, or the qualifications required of them before allowed to practice their profession."

Maisch did not content himself with the simple presentation of the information gathered. He arranged the material and commented

upon it. His "Report on Legislation Regulating the Practice of Pharmacy in the United States," (13) read at the sixth session of the Philadelphia meeting of the A. Ph. A. on September 10, 1868, (14) was a masterpiece carrying an unresistable power of conviction. There could no longer be any doubt: the time was ripe, and legislative steps protecting public welfare from possible damage by the uncontrolled conduct of pharmacy were to be expected here and there and, after some not very remote time, everywhere. If pharmacy did not take the lead in shaping its future, it was doomed to take whatever it was given.

It was the extraordinary merit of Maisch to have made this situation clear to everyone and to have pressed the cause forward so quickly and consistently that no effective resistance could be organized. The proceedings following the reading of the report on legislation proved to be a triumph obviously exceeding his expectations. At the end of the report his Committee had offered the following resolution:

"That the President and the ex-Presidents of this Association, attending this meeting, be appointed a Committee to take into consideration

1st. The propriety of drafting a law regulating the entire practice of pharmacy, to be presented to the legislatures of the different States and Territories for their adoption, together with a memorial setting forth the duties of the profession to the public and its actual and contemplated status;

2d. The propriety of inviting the cooperation of the American Medical Association and of the local Medical and Pharmaceutical Societies;

And that the Committee thus appointed be requested to report at a subsequent session."

The debate on this resolution showed that the members of the A. Ph. A. present had advanced far beyond the careful formulation offered. To them the "propriety" of a model law was beyond dispute and the suggested discussion by a Committee of dignitaries was regarded unnecessary. Nor could they see any reason for consulting the American Medical Association. Finally the following amended resolution was adopted unanimously:

"Resolved, That it is expedient to appoint a Committee to draft a law regulating the entire practice of pharmacy, to be presented to the legislatures of the different States and Territories for their adop-

tion, together with a memorial setting forth the duties of the profession to the public and its actual and contemplated status." (15)

The Committee was to report at the next annual meeting. The number of its members was restricted to the utmost, *i. e.* to only three (J. B. Moore, Philadelphia; Fr. Stearns, Detroit; Wm. Wright, Jr., New York) with Maisch and the then President of the A. Ph. A., John Milhau, as members ex-officio.

This resolution was a definite "go ahead" signal to Maisch. One year later, in 1869, he presented his "Draft of a Proposed Law" to the Chicago meeting of the A. Ph. A. (16) "Of all the subjects discussed at our last meeting," said the retiring President, Edward Parrish, in his official address, "perhaps none has since claimed so much attention in Committee and by conversation and correspondence among the members, as that of the legal aspects of Pharmacy, and the proposed enactment of laws by the several legislatures regulating the sale of poisons and prescribing what class may legally dispense medicines in the several States." (17)

The opposition was awakened and became articulate. There were those who thought the number of educated pharmacists too small for allowing any legal requirement of a certain knowledge as the prerequisite of the practice of pharmacy, and those to whom any procedure which could subject pharmacy to political influence was a matter of principle. The one group as well as the other was afraid of the burdens the suggested law would mean to the American pharmacist. To both groups Maisch had one and the same answer:

". . . Those burdens are, and were intended to be, for the benefit of the public. Directly the apothecary is not benefited by it; the one ultimately, nay directly, to be benefited is the public. If you, gentlemen, are willing as educated pharmacists to benefit the public, we all agree on that basis certainly." (18)

Maisch succeeded. It was

"Resolved, That the report of the Committee embracing the proposed draft of a law, of the action had in this Association upon that report and of these resolutions be printed in pamphlet form, and that ten copies for each State be sent to the Governors and the speakers of the legislatures of the different States of the United States." (19)

Thus the first model law of the American Pharmaceutical Association was on its way. It became, indeed, the model of a majority of the early pharmacy laws in the United States of America, and its

effect on the development of American pharmacy cannot be overestimated.

It was this success which caused similar steps in later times. In 1900, thirty-one years after the mailing of the first model laws to the legislatures of the American States, another great pharmacist, James H. Beal, prepared another model law which like its older brother was printed in pamphlet form and sent to the various State governments by the American Pharmaceutical Association. A third model law was prepared another thirty-eight years later, in 1938, by the A. Ph. A. "Committee on Modernization of Pharmacy Laws" (since 1941 "Committee on Legislative Pharmacy") under the leadership of Robert L. Swain. The final fate of this draft will certainly depend on the postwar situation.

From the very beginning it was clear to Maisch that pharmaceutical legislation, being a State affair and not a Federal one, had to be initiated, carried through, and safeguarded by those most directly concerned, *i. e.* by local pharmacists who had to be organized for this purpose. It was this conviction that led Maisch to the concept of the second idea, the realization of which proved to be of highest importance to American pharmacy.

The father of adequate pharmaceutical legislation in the United States of America became the advocate and ardent promoter of the formation of Pharmaceutical State Associations.

In his report on legislation, read before the Louisville (Ky.) meeting of the A. Ph. A. in 1874, Maisch made the following statement:

"The pharmacy laws, as they are now in force in a number of States appear to be the best carried out in those cases where an incorporated college or association is charged with the execution thereof, and it is to be hoped that where this is not yet the case, efforts may be made to effect such a change." (20)

Referring to an attempt to found a pharmaceutical association for the State of South Carolina, Maisch, in the same year, wrote in the American Journal of Pharmacy as follows:

"The effort, we trust, will prove a success, and be followed by similar earnest attempts in the other states and larger cities in which a union of pharmacists has as yet not been effected." (21)

In 1878 Maisch was personally instrumental in founding the Pennsylvania State Pharmaceutical Association.

Whenever and wherever he could, the first Permanent Secretary of the American Pharmaceutical Association inspired the organization of State Pharmaceutical Associations.

"Thus we often find," wrote the author of a historical sketch on State Pharmaceutical Associations in 1907, "that the early officers of the State organizations are also active members of the American [Pharmaceutical] Association, and that the organization of a State body followed a meeting of the American association near the birthplace of the new society." (22)

It was in 1880 that Maisch under the heading "State Pharmaceutical Associations" triumphantly stated the following:

"To have attempted the formation of such associations a few years ago would have been thought entirely unnecessary; and now there is scarcely a State where such a society is not either in progress of formation or being urgently called for by many of the craft." (23)

Those in American pharmacy who had gone at least some part of the way with Maisch knew that his work as the first Permanent Secretary of the American Pharmaceutical Association would, in the course of events, outweigh all his other activities important as they were at their time. When the painful illness leading to his death prevented Maisch from attending the 1893 meeting of the A. Ph. A. at Chicago, which simultaneously was the seventh in the series of International Pharmaceutical Congresses and the first one held in America, the Association unanimously adopted and conveyed to Maisch the following resolution:

"The American Pharmaceutical Association assembled, conveys to you the heartiest greetings and the sympathy of its members in your sufferings. They keenly feel and regret your absence, and trust that you may find consolation in the knowledge that their love and esteem are with you, and that your eminent and enduring services for the promotion of the Association and for the elevation and advancement of pharmacy will ever remain an ornament in the annals of American pharmacy." (24)

In his reply Maisch said the following:

"If those kind words are the sentiment of the profession, then surely I may entertain the hope, which at this time of trial and suffering is a consolation and a satisfaction to me, that my labors in the past have not been entirely in vain." (25)

The organization of American pharmacy as a recognized part of public welfare with as little restriction of the individual liberty of the pharmacist as possible has to a great extent been the fruit of John Michael Maisch's "labors in the past."

Like his famous compatriot and fellow revolutionary, Carl Schurz, he knew that real liberty can be preserved only on the basis of order and responsibility. Carl Schurz made this idea fruitful for the great Commonwealth in which we are living as Secretary of the Interior of the United States of America. John M. Maisch did the same for the professional unit to which he had devoted his lifework as Secretary of the American Pharmaceutical Association. Each of these Secretaries did his job well.

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INFLATIONARY BORROWING

By Karl Scholz, Ph. D.*

WHEN the Federal government cannot raise the necessary revenues to finance the huge war expenditures by taxation and borrowing of current incomes, it can get additional dollars by borrowing from commercial banks and Federal Reserve banks. Such borrowing is apt to be distinctly inflationary. The dollars obtained from the banks are in the nature of new money or manufactured currency.

Under the American banking system banks may lend more dollars than have actually been deposited with them, on the assumption that not all depositors will want to withdraw their funds at the same time. This is known as the principle of fractional reserves. The reserves of a bank represent their non-earning assets, while deposits of clients are liabilities of the bank. Since experience has taught us that banks can lend more "money" at any one time than they hold in reserves, they can increase their earning assets by extending loans to clients, in the form of deposit credits, against which the clients can draw their checks with which to pay their bills. Under our banking laws, commercial banks may lend on an average five dollars of deposit money for every one dollar of lawful reserves. Since these lawful reserves are ultimately based on gold dollars, the number of such gold dollars in our money stock sets a limit to the number of deposit dollars a bank may lend.

As a result of reducing the amount of gold in the American dollar after 1933 by raising the price of gold from $20.67 per ounce to $35.00 an ounce and the subsequent large importation of gold, our monetary gold stock by 1940 had reached the huge sum of over twenty-two billion dollars, or more than seventy per cent, of the monetary gold of the whole world. Banks had seven billion dollars of reserve money in excess of what the law required to be held as security against their clients' deposits. When the government needed additional dollars to finance the expanding war program, it could therefore borrow from the banks, and the banks could lend credit currency to the government by expanding their deposits.

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When John Doe writes a check for $1000 against his bank account to buy a government bond, his deposit is reduced by $1000, while the United States Treasury's deposits are increased by $1000. As the government uses these $1000 to pay its bills the funds find their way into someone else's deposit account, but the total bank deposits are not increased by such a lending transaction but are merely transferred. On the other hand, when commercial banks buy government bonds, and credit the United States Treasury account (either directly or indirectly) with a deposit equal to their purchase of bonds, the total deposit currency of the country tends to increase correspondingly.

This is what is known as inflationary borrowing. It threatens to raise prices all along the line, particularly at a time of approximately full employment of our productive resources, and the shrinkage in the supply of saleable consumers goods, because of diversion of these resources to the war effort. In 1941, the Federal government borrowed twenty-five billion dollars from commercial banks and Federal Reserve banks, and in 1942 approximately twenty-four billion dollars. The effects of such inflationary borrowing may be concealed for the duration by rigorous price controls and rationing. But this does not remove the dangers of price inflation at the close of hostilities if the governmental brakes should be released. As a matter of fact, wartime inflationary borrowing accentuates the dangers of post-war price inflation, since it helps the accumulation of idle dollars in the pockets of the people.

Unless the excessive current incomes, generated by production for total war, can be absorbed through taxation and voluntary as well as compulsory saving in sufficient amounts to meet the war costs, further inflationary borrowing from commercial banks will become necessary. All these additional funds exercise a continuous upward pressure on prices, which cannot be held in check indefinitely, without increasing governmental regimentation, coercion and control.

The consequences of rising prices, induced by inflationary borrowing, are becoming increasingly obvious to more and more people. Those living on fixed dollar incomes are seeing the buying power of their money diminish. Increasing taxes on their shrinking incomes is analogous to adding insult to injury, when others are having their dollar incomes adjusted upward to meet increasing living costs.

If postwar price inflation, brought on by wartime currency expansion, should be allowed to take its course, we may be faced with

a pronounced decline in the value of our life insurance policies, our social security benefits, the incomes of endowed institutions, and above all, the integrity on which our credit system rests. If debts can be repaid with relatively cheap dollars, the inducement to save and invest dollars to provide for the future will be undermined, while more and more people will look to government for protection and security. The serious consequences of continued inflationary borrowing should be clearly recognized by all our citizens. Only by making the necessary sacrifices now to win the war, on the part of all the people, can we avoid the real dangers of losing the peace through postwar price inflation.

Reports of the Progress of Applied Chemistry. Vol. 27, 1942. 551 pages. Society of Chemical Industry, London.

This volume, issued by the Society of Chemical Industry annually, summarizes the progress made in the field of chemistry and chemical engineering. The amount of published information available again shows a falling off due to abnormal conditions as noted last year.

This section of the annual report deals with the aspects of industrial chemistry known as chemical engineering. The subjects treated are classified as the ordinary unit operations of chemical engineering. Under diffusional operations are grouped those subjects dealing with mass transfer across a fluid boundary. Those operations which utilize mechanical energy as well as diffusional forces are separately grouped, and followed by the purely mechanical operations such as size reduction. At the end of the review are two isolated sections dealing with water treatment for boiler work and constructional materials.

Although the war has affected the quantity of material to be presented it has not affected the quality of the presentation.

The chapter on fine chemicals and medicinal substances begins with the shortage of quinine due to the fall of Java; discusses the new substances added to the British Pharmacopœia; summarizes the anti-bacterial substances, the diamidines, the sulfonamides and sulfones, the acridine derivatives, the vitamins and so on down the line.

M. O. H.

RATIONING, OUR DIET, AND SOUND NUTRITION

By T. Swann Harding

WARTIME rationing now seriously affects our supply of fats and proteins. The former are energy foods which contribute calories, primarily, though carbohydrates will to some extent replace them. They also act as vehicles for the fat-soluble vitamins. Proteins build our muscle or lean-meat tissues and are found primarily in meat, milk, and eggs, secondarily in vegetables, nuts and cereals.

Proteins are complex chemical substances made up of different combinations of a score or so of simpler compounds called amino acids. Some of these amino acids are called essential, because our bodies cannot manufacture them if we lack them in our diets; some are nonessential because our bodies can synthesize them.

Good proteins are those high in the essential amino acids, and the proteins of meat, milk and eggs are outstandingly good. Most vegetable proteins contain inferior selections of amino acids and this limits their biological usefulness.

As long as we live there is a constant build-up and tear-down of our tissues. This is called metabolism. We need a certain quantity of protein daily to help rebuild worn-out or torn-down tissues, but just what quantity is still a moot question. Neither mental nor physical exercise really tears down much lean muscle tissue. Some authorities hold that we need very little replacement protein indeed. But we should not depend heavily on protein for energy in any case.

A good protein is a good protein, no matter from what it is derived. Meat is meat, and no special nutritive virtue resides in so-called "red" meats. The protein of fowl, fish, milk, cheese, eggs, or even of some nuts, is just as nourishing as that of beef, pork or lamb. A hard worker may imagine that he must gorge himself on "red" meat to keep up strength, but that belief is largely based on illusion.

What will rationing of meats and fats mean in terms of our diet? It will mean that overfed, well-fed, and expensively fed Americans must adopt the dietetic standards hitherto reserved for lower-income groups. Under peacetime conditions a third of our population lacked enough ration coupons in the form of dollar bills to purchase a diet rated good by nutrition scientists.

Others of us were at the same time well fed, overfed, or merely expensively fed. The last term is used because it is perfectly possible to pay high prices for a luxury diet that is nevertheless deficient nutritionally. Many Americans long managed to do just that.

During peacetime days Dr. Hazel K. Stiebeling and her associates in the Department of Agriculture graded diets as liberal, moderate, and barely adequate. Only the first of these amply satisfied all nutritional standards of full adequacy. Under rationing this diet disappears for the duration, for no one will have sufficient coupons to afford such a diet.

The moderate diet, upon which most Americans in the middle and middle-upper income brackets lived, is procurable on the ration coupons now issued. But it will take sound knowledge of nutrition science, skilled management, and intelligent attention to food purchasing and the conservation of nutritional values to maintain it. There must be as little waste as possible in cooking, serving and consuming food.

The minimum-subsistence diet, which Dr. Stiebeling presented in three variations for low-income families, can also be maintained on our ration coupons. Few changes must be made in it. Yet not all families in the United States will be able to purchase even it. If they were all able to do so we should have insufficient food to provide it universally. It is a melancholy fact that many of our people will fall below this level of subsistence, even as more of them did when we were at peace.

Under the present rationing system some of us must drastically reduce our consumption of protein and fats from animal sources. Yet relatively few of us will be called upon to do so, for the vast majority of our people already lived on minimum-subsistence diets, or less. A few figures in terms of pounds of food consumed per person per year will not be amiss here.

Whereas in the 1935-39 period, we consumed beef at a per capita rate of 55 pounds yearly, this rose to 60½ pounds in 1941-42, and the demand would be 73 pounds this year, without rationing. Instead our allocation is 57 pounds per capita. In the 1935-39 period we consumed 806½ pounds per capita per year of milk and milk products—butter, cheese, cream, fluid milk, etc.—which jumped to 852 pounds in 1941-42. Without rationing demand would take 885 pounds in 1943 which rationing cuts back to 769.

Since 1935 we have been accustomed to consume about 50 pounds of food fats yearly. Our 1943 ration will allocate us but 45 pounds. Our egg supply will be higher this year than in the 1935-39 period, about the same as in 1941-42, but somewhat less than we should consume if supplies permitted.

In 1943 civilians received 80 per cent of the butter and the veal, the rest going to the armed forces and Lend-Lease. They also got 73 per cent of the condensed milk, 70 of the eggs, 68 of the canned vegetables—soups included, 66 of the beef, and 65 per cent of the lamb and mutton. But civilians were allocated only 55 per cent of the available cheese, 43 of the evaporated milk, 14 of the dried whole milk, 53 of the canned fruits and juices, half of the dried beans, 40 per cent of the dried peas, and 59 per cent of the pork.

In quantity terms this means that civilians received more dried whole milk, canned vegetables—soups included, pork, eggs, condensed milk and dried peas than they had during the 1935-39 period. But they had less, and in some cases drastically less, butter, evaporated milk, dried beans, beef, cheese, dried skim milk, canned fruits and juices, veal, lamb and mutton. This is the dietary picture as briefly as it can be presented.

We must never forget, though, that we live in a country which has never seen fit to produce, process and distribute enough food to provide all its inhabitants with an adequate diet. Yet it has cultivated the myth of food abundance. Now that the home front is merged with the fighting front food shortages bother righteous citizens who never considered our chronic food scarcity of past years of peace.

Many foods started out as upper-class luxuries, became comforts, then were regarded as necessities by those who could afford them. These often were consumed to satisfy appetite and not for their nutritive value, which was low. Upper-income people habitually overate. Rationing will curb that tendency, though it will be impotent to enable all who formerly ate too little to procure adequate diets.

Nevertheless many families and individuals who ate expensively failed to procure nutritionally adequate diets. Malnutrition existed among upper-income groups as was shown in a recently published study of diets consumed by some of them. They consistently ate too little protein and too much fat. While only one in ten of them got sufficient carbohydrates, nine out of ten of them got too much fats,

and over a third of them ate insufficient proteins to meet nutrition standards.

Three-quarters of these well-to-do people got insufficient calories or energy in their diets and just as many had too low an intake of parts of the important vitamin B complex. Nine physicians among these people had diets as deficient as any of the rest. It was concluded that high incomes induced people to consume rich, fatty foods that those on low incomes could not afford.

The foods these better-income individuals lacked most frequently were milk, eggs, fruits and whole-meal or properly enriched cereal products. It was also felt that their average single daily serving of meat provided insufficient protein. Such persons merely lack the knowledge or the desire to select good diets. Further popular education in nutrition is indicated.

But many Americans have been going underfed simply because they could not afford to purchase an adequate diet. A poll by the American Institute of Public Opinion, announced February 7, 1943, indicated that, even though they had higher wages and more work than for years, most Americans consumed insufficient protective foods —citrus fruits, raw greens, eggs and dairy products. More than a third of all adults appeared to consume no milk and no cheese at all.

But the lower the income the greater the dietary deficiency. While less than a quarter of those in upper-income groups had insufficient citrus fruits and greens, more than half those in lower-income groups had diets deficient in these. While 7 per cent of those in the upper-income group were deficient in meat, fish and poultry, 15 per cent in the lower-income group were. But practically everybody got sufficient cereals and bread.

A striking account also appeared not long ago covering a survey of the diets of 7,000 children from nearly 4,000 families with incomes varying from $10,000 a year down to relief status. Gross physical manifestations suggestive of poor nutrition were discerned in 60 per cent of these children, and the dietary patterns of three-quarters of them were below the level of minimum adequacy. But, while 92 per cent of the diets were inadequate at the relief level, only 41 per cent were at the highest levels of family income.

The diets of three-quarters of the white children were below recommended allowances in fruits and vegetables, though the deficiency was 98 per cent among children from the poorest families.

Protein was rarely deficient at any income level. Other studies confirm the fact that children from families with above-average incomes usually have inadequate diets and are in poor nutritive condition.

All classes then have neglected the newer knowledge of nutrition, the revelation that vitamins and minerals play a vital role in our diet. This is not wholly true, of course. For, in the period that elapsed between 1909-13 and 1935-39, we as a nation so changed our food habits as to consume 13 per cent less meat, 23 per cent less potatoes and 32 per cent less cereals, but 12 per cent more fruit, 11 per cent more vegetables other than potatoes, and 19 per cent more dairy products.

In general, we consumed 5 per cent fewer calories in the latter period, 17 less carbohydrates, and 16 per cent less protein. Our consumption of fats and oils increased slightly. Thus we were slowly putting the newer knowledge of nutrition into practice.

Yet our annual meat bill has been rather an imposing thing. We usually spent more for meat than for clothing, though we were supposed to be the best dressed people in the world. We spent seven times as much for meat as for bread, five times as much as for public schools, ten times as much as for churches. Much of this meat was eaten unnecessarily, insofar as good health and a normal activity level were concerned. Too much of it went to people with higher incomes.

Nutrition scientists generally hold that adults should consume from two and one-half to three ounces of food protein daily, which may be regarded for present purposes as equivalent to lean steak. But some of them have held that two ounces was sufficient and others that four would be more like it. However, when a thousand people on ordinary diets were studied, it was found that about one in ten of them somehow got along on two-thirds of an ounce of protein daily, though one and one-half ounces is usually regarded as a barely safe minimum.

It was astonishing that only 7 per cent of these people ate two and one-half ounces or more of protein a day, nine out of ten of them ate two ounces or less, and six out of ten ate less than one and one-half ounces. Yet these were "normal" people consuming their accustomed diets. Though such low-protein rations are considered unhealthful, they were getting along. Females dominated the low-

protein and males the high-protein group and, incidentally, blood pressure appeared to be unaffected by protein intake.

Meat also has accessory value in our diet other than its protein content. Many animal tissues, liver especially, are good sources of iron and copper, and of certain vitamins. But we can procure plenty of vitamins and minerals from fresh fruits, vegetables, cereals and dairy products. Salads are not "sissy" foods, though often neglected by "he-men." The enrichment of flours, cereals, breads and butter substitutes with vitamins and minerals does much to compensate for any deficiency caused by a lower meat intake, and this enrichment can be made very cheaply.

However, vegetable and cereal proteins are not generally as good as meat proteins, and vegetable fats, even after vitamins are added, are somewhat inferior to butter nutritionally, at least for growing young. Yet it is quite possible to maintain life and a fair degree of health and activity on a purely vegetarian diet. Many individuals and many tribes have proved this, though a considerable number of so-called vegetarians consume animal proteins in the form of eggs and dairy products. Health is not adversely affected by vegetarianism.

Furthermore, experiments with laboratory animals have shown that the life span can be doubled by using a low-protein diet to retard growth and the advent of maturity. There is considerable evidence that overfeeding children to promote quick physical maturity is not conducive to good health or longevity as adults. Just how much it would be worth to starve ourselves somewhat in order to live longer each must figure out for himself.

Our present rationing system will, nevertheless, provide enough beef, pork and lamb, along with unrationed fowl, and fish—to supply sufficient protein for those who can afford to buy as good a diet as the ration coupons will permit. We also have good accessory sources of protein in rationed cheese and in eggs, peas, beans, lentils and many other vegetables. We can still have a nutritionally satisfactory, if not a highly palatable, diet if we have the cash to buy it.

But, if we are to continue feeding millions outside as well as inside the United States, we may soon have to consider a revolution in our agriculture. For the pounds of human food produced by most animals per hundred pounds of digestible matter they consume is not impressive. That means less dependence on livestock and more on cereals, which is the universal trend under population pressure.

A milk cow produces only about eighteen pounds of food per hundred pounds of digestible nutrients consumed, but the figure for dressed beef is only nine and one-half pounds; for pork it is fifteen and one-half pounds but for veal only eight; for dressed poultry it is only a little over four and for lamb three pounds. An animal returns about five and one-half pounds of butter and five of eggs per hundred pounds of digestible nutrients fed.

While an acre of soil under potatoes will produce about 4,000,000 calories for human consumption and under wheat 2,000,000, it produces only 666,666 calories if used to graze milk cows, and a mere 200,000 when grazing beef cattle. Hence, if a tremendously larger number of people must derive subsistence rations from American arable acres, we must depend less on livestock and more on cereals, poultry, eggs and dairy products.

Our diet would then contain a minimum of animal protein. We should derive most of our energy from bread grains and cereals, and our diet would be richer also in fresh fruits and vegetables than it has been in the past.

Good protein would be derived from poultry, eggs and dairy products, as well as from old cows and from sheep raised primarily for wool. We should use the fish of the sea and inland waters more and the production of the latter could be increased considerably by stocking ponds and rivers. We should also have cattle and goats produced on range land unfit for cultivation.

Our diet could then be produced with minimum land and labor. It would be wholesome, if not excessively palatable. The general adoption of this diet would enable us to support a very much greater population than we ever thought possible. Psychological factors would interfere with the adoption of such an agriculture, and the diet it produces, in time of peace, would be altered in wartime.

There is good reason to think that our farm production can be increased little during the war, provided we stick to the old plan, and the customary composition of output. It may actually decrease. Moreover, we shall doubtless have to ration food for some time after the violent phase of the conflict is over, and that may take some years. Certainly we cannot cope with the problem of feeding war-torn nations unless we convert our agriculture specifically to the intended purpose.

We normally derive about 60 per cent of our protein from milk, meat and eggs; we can do very well nutritionally, however, if we derived but 30 per cent of it from animal sources. We usually derive 41 per cent of our calories from likestock products, 32 per cent from cereals, principally wheat, 8 per cent from dry legumes like peas, beans and soybeans, 4 per cent from potatoes, 2 per cent from other vegetables, 4 per cent from fruits, 6 per cent from sugar crops, and 3 per cent from cottonseed oil.

In 1942 we produced enough calories to provide 115 per cent of our national needs, as consumed, leaving 8 per cent for industrial uses. The surplus went to the armed forces, Lend-Lease, overeating and waste. But, if we had fed to human beings the grains we produced that year and fed to livestock, we should have provided 270 per cent of our national caloric requirements. Yet, in the form of livestock, this feed, along with hay, roughage and waste eaten by the animals, provided for only 47 per cent of our national needs in calories.

This means that we must veer towards the production of foods which make the most efficient use of our farm resources and those are, primarily, non-animal foods. Animals are efficient in converting material inedible by human beings into food that human beings relish. On a strict conversion basis also, a laying hen compares unfavorably with a pig, though eggs have a more important dietetic role than bacon. The fact remains that an average acre of arable land will feed more human beings or animals than an acre of grassland.

An acre of pasture will produce about enough meat for one person. Under the plow it will produce wheat enough for twenty-one or potatoes enough for forty-two persons. Bread, potatoes and sugar beets produce food energy in large quantity, and we can get along very well indeed when deriving 60 per cent of our energy from carbohydrates and only 25 per cent from animal fats and 15 per cent from proteins.

As the war continues, or while we have to feed many outside of the United States, we should greatly increase our consumption of leafy green and yellow vegetables, potatoes, sweet potatoes, dried beans, dried peas, soybeans, nuts, tomatoes, citrus fruits, and whole milk and its products. We should significantly decrease our consumption of sugar, meats, animal fats and of vegetables other than those just mentioned. Such a diet would nourish us well under

rationing and would also make the most efficient use of our farm resources.

Finally we could create a great deal more food for ourselves merely by curbing waste. About 15 per cent of our food goes into the garbage, and this figure does not include inedible waste. It is estimated that restaurant management wastes from 3 to 8 per cent of the food purchased and patrons leave about 6 per cent on their plates. Food waste runs from 6 to 8 per cent in retail stores. In general, food loss, between the time of production and the time it leaves the retail store, averages 30 to 40 per cent.

In 1942 we wasted as much food in homes as was set aside for our armed forces and Lend-Lease shipment together. We could, therefore, more easily increase food production by starving the garbage can than in any other way. A slice of bread saved weekly in each home would mean two million more loaves of bread to eat weekly. A half ounce of butter saved weekly by each person, and that much was wasted in 1942, would have provided sufficient of this food for our armed forces that year.

Convert agriculture still further, continue rationing, and end food waste—that is the formula for giving an adequate diet to far more people than we have ever fed before.

SELECTED ABSTRACTS

Patulin in the Common Cold: Collaborative Research on a Derivative of Penicillium patulum Bainier. H. Raistrick *et al. Lancet 2,* 625 (1943); through *Pharm. J. 97,* 202 (1943) and *J. A. M. A. 123,* 1120 (1943). Patulin, which is anhydro-3-hydroxymethylene-tetrahydro-γ-pyrone-2-carboxylic acid, has been isolated in pure crystalline form from filtrates of cultures of two strains of *Penicillium patulum* Bainier grown on synthetic liquid media.

The substance crystallizes from ether in large colorless prisms or thick plates, m. p. 111° C. It is optically inactive, and is soluble in water and most of the common organic solvents except light petroleum benzin. The aqueous solution is neutral to litmus, and does not titrate as an acid.

It completely inhibits the growth of *Staphylococcus aureus* at a concentration of 1:64,000, and partially inhibits growth at 1:128,000.

In vitro experiments demonstrated that patulin exhibits bacteriostatic properties against both gram-positive and gram-negative organisms, although its activity against the former is much less than that of penicillin.

Clinical experiments on a group of nearly 100 patients and eighty-five controls suffering from common colds were performed. A solution of the drug was either sprayed into the nose and throat or was sniffed up from the palm of the hand. Fifty-seven per cent of the treated cases recovered completely within forty-eight hours, as compared with only 9.4 per cent of the controls. No ill effects were observed.

It is emphasized that no definite claims can be made for patulin until additional clinical data have been secured. The material for such trials will be supplied in England by the Therapeutic Research Corporation under the brand name "Tercinin."

Use of Sodium Fluoride for Desensitizing Dentin. W. H. Hoyt and B. G. Bibby. *J. A. D. A. 30,* 1372 (1943). The efficacy of sodium fluoride as an obtundent for sensitive dentin was first

demonstrated by Lukomsky in 1941. The authors treated a series of twenty patients with local applications of a 4 per cent aqueous solution of the chemical, noting that some degree of desensitization was produced.

Highly satisfactory results were obtained through the use of a paste consisting of equal parts of sodium fluoride, white clay, and glycerin. In a series of seventy patients so treated only two failures were observed, and in these two patients it was noted that other teeth responded favorably. Treatments were found to be less effective in areas of teeth showing marked hyaline dentin. Confirmation of the results noted has been received by the authors from other observers.

A standardized method of application was worked out. The area to be treated was first cleansed with cotton moistened with a 4 per cent aqueous solution of sodium fluoride, and then isolated with cotton rolls. A small quantity of the 33 per cent paste was applied to the sensitive surface by means of a plastic instrument and rubbed vigorously until all sensation disappeared; this required from one to five minutes. Some patients experienced acute pain during this operation; in such instances the paste was washed off with a warm spray, after which a second paste treatment could be given without difficulty. After desensitization had occurred, the paste was removed by washing with a spray and a rinsing of the mouth by the patient.

The effects of the treatment last for many months, varying with the patient.

It is suggested that this treatment should be used with caution, pending further research on refinements of technic in administering it.

The Assay of Penicillin. U. Wilson. *Nature 152,* 476 (1943); through *Pharm. J. 97,* 202 (1943). The inhibition by penicillin of the growth of a suitable group A β-hemolytic streptococcus, using a 5 per cent suspension of washed sheep cells as indicator, furnishes a rapid method of assaying penicillin.

The penicillin to be tested is diluted to about 1 unit per mil. By means of a micrometer syringe 0.20—0.10 quantities in 10 per cent steps are measured into 8 cm. x 1 cm. tubes containing 1 mil of nutrient broth. To each tube is then added 0.2 mil of a suspension of 500-700 x 10 organisms per mil and 0.8 mil of sheep cells.

The contents of the tubes are then mixed by inversion and incubated in a water bath at 37° C. for from three to three and one-half hours. They are then centrifuged and read for hemolysis. A suitable standard and controls are included with each rack of tests.

Phenylmercuric Nitrate: Chemical and Bacteriological Notes. D. N. Gore and R. M. Day. *Pharm. J. 97,* 172 (1943). As a basis for the quantitative assay of phenylmercuric nitrate the authors suggest the reaction between one molecule of this substance and five equivalents of iodine in the presence of potassium iodide. An accurately weighed sample of approximately 0.2 gm. is dissolved in 100 mils of 70 per cent alcohol with the aid of heat. The solution is then cooled, and to it are added 25 mils of N/10 iodine, whereupon a finely divided precipitate of phenylmercuric nitrate appears. After this has redissolved, 200 mils of cold water are added; the excess iodine is titrated with N/10 sodium thiosulfate, using starch solution as indicator. Each mil of N/10 iodine is equivalent to 0.01268 gm. of phenylmercuric nitrate. It is necessary to run a blank determination on the alcohol, since iodine reacts with this substance to an appreciable extent.

The experimental error in five determinations ranged from —0.51 per cent to +1.00 per cent.

In order to conduct sterility tests on a parenteral preparation which contains phenylmercuric nitrate, it is necessary to inactivate this inhibitory agent by some means, preferably by its reaction with iodine. Several experiments in which the organism used was *Bacillus subtilis* were performed in order to compare the results obtained by chemical inactivation of phenylmercuric nitrate with those observed by following the dilution method of the B. P. Appendix.

The results indicated that the latter method is unreliable as a sterility test where phenylmercuric nitrate is involved.

Effect of Storage of Citrated Blood on the Survival of Transfused Erythrocytes. J. F. Ross and M. A. Chapin. *J. A. M. A. 123,* 827 (1943). It has previously been shown that the radioactive isotope of iron Fe^{59} is incorporated into the hemoglobin of newly formed erythrocytes when it is administered to patients exhibiting the hypochromic anemia of iron deficiency, and further that it is liberated only when the cell is finally broken down.

In this study such patients received iron containing the radioactive isotope either orally as ferrous sulfate or intramuscularly as ferrous ammonium citrate. The counts were recorded with a modified Geiger-Müller counter and scaling circuit. After sufficient radioactive iron had been incorporated into the erythrocytes of the donor subjects, samples of blood were withdrawn by venesection into sterile sodium citrate solution. The donor blood was then divided into aliquots and stored under sterile conditions in the refrigerator for periods varying from one to fourteen days, during which time hematologic studies and determinations of radioactivity were carried out on aliquot portions.

After such storage aliquots of the labeled blood were injected into healthy human adults who possessed normal erythrocyte and hemoglobin levels. Solutions of Evans blue dye (T-1824) were injected immediately prior to the blood transfusion, in order that the plasma volume could be determined. Thereafter, at varying periods, samples of venous blood were withdrawn for hematologic study and determination of the dye content of the serum and of the radioactive iron present in the blood and in the cell mass. From the data obtained the total radioactivity in circulation at the time of withdrawal of the sample and also the percentage of the total transfused labeled cells in circulation at any given time were calculated.

It was found that the destruction of the transfused erythrocytes was rapid immediately after injection, but that it subsequently progressed at a slower and steadily decreasing rate. Prolongation of storage greatly increased the rate of destruction of the transfused cells, the percentage surviving for twenty-four hours varying inversely with the length of storage time. The observations confirmed the findings of other investigators that citrated blood is unsatisfactory for transfusion when it has been stored for more than two or three days.

It was noted that the breakdown products of hemoglobin are rapidly and preferentially reutilized for the synthesis of new hemoglobin, a fact which made it impossible to trace with accuracy the survival of the radioactively labeled erythrocytes for more than forty-eight hours after transfusion.

SOLID EXTRACTS

A most effective lotion for the eradication of head lice was recently reported in the *Journal of the American Medical Association.* It has the following formula:

Phenyl Cellosolve	40 parts
Ethyl Alcohol	30 parts
Methyl Salicylate (as a perfume)	5 parts
Water	25 parts

It should be applied so that the hair is thoroughly wet but it must not be permitted to get in the eyes. A single treatment is said to be 100 per cent effective.

AJP

The mental damage wrought by modern warfare is good evidence of the terrible fury of modern intensive combat operations. In spite of the careful screening of all men entering the armed services to weed out the mentally weak, twenty to twenty-five per cent of all hospital admissions following combat are due to neuropsychiatric disorders—in other words, mental damage.

AJP

From 50 to 70 per cent of such cases recover in from two to five days and return to combat duty. One of the most effective treatments is getting the soldier to talk about his harrowing experiences which seems to relieve his pent-up emotions and brings mental relaxation.

AJP

Diasone is a new substance which has been used with very promising preliminary results in the treatment of tuberculosis. This is especially encouraging in this season of the year when we have been buying Christmas Seals and affording revenue for the noble fight against this dread disease.

Have you been of the opinion that scientists and the general public have forgotten about television, at least until after the war? Not so. Those scientists who are available are still perfecting their work in this field, and the broadcasting companies are still quite interested, with regular daily programs being telecast. In the New York area there are about 5000 sets, 89 per cent of which are still in good working order. In a recent survey conducted by the National Broadcasting Company, and reported in the magazine *Tide,* 1113 homes which had television sets have audiences averaging eight persons for the favorite shows, and about three-quarters of the 155 public places which reported television sets averaged audiences of forty-six people.

AJP

Rather than risk the danger of surgery under highly unfavorable conditions at sea, acute appendicitis may be treated by chemotherapy. A recent paper in the U. S. Naval Medical Bulletin *reported that eight cases positively diagnosed as acute appendicitis were treated with sulfathiazole given orally. All cases showed a progressive diminution of pain, tenderness and rigidity and the white cell count progressively decreased. The authors do not recommend this procedure as superior to surgery but far superior to either unskilled surgical attempts or surgery under septic or other dangerous conditions.*

AJP

Glycosuria, or the lack of it, of course, has never been considered a criterion for the diagnosis of diabetes but neither is the customary glucose tolerance test an infallible test for diabetes. In a few instances obese individuals give a typical diabetic glucose tolerance curve but after their weight is reduced to normal they are found to have a perfectly normal glucose tolerance.

AJP

The rather widespread practice of using sulfonamides in the treatment of the common cold is both endorsed and condemned by the medical literature. Some workers claim that the course of the cold is unaffected by such therapy and that therefore the use of such potentially dangerous drugs is unwise. Others favor the use of the sulfonamides in severe colds largely as a prophylactic measure to prevent serious secondary infection.

BOOK REVIEWS

The Biochemistry of Malignant Tumors. By Kurt Stern and Robert Willheim. Reference Press, Brooklyn, N. Y., 1943. 885 pages text, 64 pages author and subject index. Price: $12.00.

This book represents the most extensive survey of the results of biochemical cancer research as yet published in the English language. The literature of the last twenty-five years, up to the beginning of 1942, is systematically covered.

The term biochemistry is used in a broad sense. In addition to chapters on inorganic, organic and physical chemistry, enzymes, nutrition and metabolism, the book includes sections on immunology, endocrinology, biochemistry of tumor origin and tumor growth, and chemical and biological diagnosis of cancer. Emphasis is placed upon providing detailed objective information as to the results and opinions of the different investigators in these fields although efforts are made to reconcile contradictory statements or to enumerate reasons for the discrepancies.

The great merit of this book lies in the completeness of the bibliography. As far as the reviewer is able to judge, there is no physical or chemical method of propagating, treating and diagnosing cancer that is not adequately discussed in this treatise. The shortcomings are in the theoretical sections, especially in the chapter on metabolism, where some errors and misinterpretations occur.

While this book should not be considered a critical review of biochemical cancer research and while it will not eliminate for the student of cancer the trouble of reading the original papers and forming his own conclusions, it can be recommended as a highly desirable volume of reference for the library of the cancerologist.

OTTO ROSENTHAL

Manual of Laboratory Glass-Blowing. By R. H. Wright, Associate Professor of Chemistry, University of New Brunswick. Chemical Publishing Co., Inc., 234 King Street, Brooklyn, N. Y., 1943. ix + 90 pp. Illustrated. Price: $2.50.

Following a brief discussion of the various types of glass, burners and a description of tools employed in glass blowing, the usual fundamental operations are described. These operations are illustrated with photographs. A splicing torch for the assembling of complex apparatus is also described and illustrated.

Under advanced operations are included the making of bulbs, ring seals, condensers, thermometer wells, glass diaphragm manometers, vacuum jackets, closed circuits of tubing, mercury vapor pumps and a McLeod gauge. Directions are given for sealing in wires and the preparation of ground joints. Mention is made, also, of the use of graded seals.

The manual should prove useful as a guide to the beginning glass blower.

N. Rubin

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The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

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Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

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